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ORIGINAL ARTICLE

Oxidation-stable linoleic acid by inclusion in α-cyclodextrin

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Abstract Linoleic acid is essential to the skin's barrier function. Its skin-care and restorative properties make it attractive for use in cosmetics and dermatology. However, its sensitivity to oxidation and tendency to go rancid prevent its use in cosmetic preparations. But in the form of a molecular inclusion compound with α-cyclodextrin, linoleic acid is effectively protected against oxidation. Investigations into the storage and light stability, olfactory tests and headspace analysis of the formulations give evidence of the stability of a suitable inclusion compound. Reversible complexation makes it possible for the first time to use linoleic acid in various cosmetic formulations and personal-care products.

Keywords Vitamin F · Linoleic acid (LA) · Polyunsaturated fatty acids · Skin care · Cyclodextrin (CD) · α-cyclodextrin/linoleic acid complex

Introduction

Lipophilic vitamins such as retinol, tocopherol and linoleic acid (LA) form inclusion complexes with native cyclodextrins (CD). Retinol [1] was found to build inclusion compounds with γ-CD in a molar ratio (guest/CD) of 1:1 and 1:2, while tocopherol [2] does so in a molar ratio (guest/CD) of 1:1, 1:2 and 1:3. Linoleic acid [3] forms inclusion compounds with α-CD in a molar ratio (guest/CD) of 1:1, 1:2, 1:3 and 1:4.

Linoleic acid is essential to the skin's barrier function [4]. Its skin-care and restorative properties make it attractive for use in cosmetics and dermatology. If the skin lacks linoleic acid, its barrier function will be disrupted and there will be a higher rate of trans-epidermal water loss; the skin becomes dry, scaly and turns an unhealthy color. This fatty acid is essential for the human body; a greater amount of linoleic acid is needed after serious accidents and in certain diseases. A daily intake of 8–10 g is recommended for adults [4].

However, its sensitivity to oxidation and tendency to go rancid prevent the use of this polyunsaturated ω-6 fatty acid (PUFA) in cosmetic preparations. A mixture of polyunsaturated fatty acids (PUFA) is often named "vitamin F" in the food and cosmetics industry. Vitamin F contains polyunsaturated ω-6 and ω-3 fatty acids with chains of 18 or more carbon atoms and at least two double bonds. The main ingredient of vitamin F is linoleic acid, whose systematic name is *cis,cis*-9,12-octadecadienoic acid.

In the form of a molecular inclusion compound with α-cyclodextrin, however, linoleic acid is effectively protected against oxidation. Investigations into the storage and light stability, olfactory tests and headspace analysis of the formulations show that a suitable inclusion compound is stable. Reversible complexation opens up the possibility for the first time of using linoleic acid in various cosmetic formulations and personal-care products.

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Materials and methods

Materials

Linoleic acid was purchased from Aldrich. α-Cyclodextrin is a product of Wacker Chemie AG, Munich, Germany.

Methods

The inclusion compounds were prepared from concentrated cyclodextrin solutions or by the kneading method with the exclusion of light and under nitrogen atmosphere. The ratio of linoleic acid/α-CD was measured by proton NMR, the content of linoleic acid in formulations by GC. The chemical shift of the integrated peak for linoleic acid was at 5.3 ppm and for α-CD at 4.8 ppm. Spectrometer used: Bruker Advance DPX 400 (frequency for 1H 400.13 MHz), solvent DMSO-d6 + trifluoroacetic acid, acquisition parameter: NS = 64 (number of scans), TD = 64k, O1 = 3,088 Hz (at 500 MHz); 1.601 Hz (400 MHz), SHW = 10,330 Hz (at 500 MHz!); 8,013 Hz (400 MHz); pulse program = zg30, D1 = 2 s, T = 25/27 °C; processing parameter: SI = 32K, WDW = EM, LB = 0.3 Hz. The principle of the method was silylation by MSHFBA (*N*-methyl-*N*-trimethylsilylheptafluorobutyramide). GC operating conditions were (a) instrument: gas chromatograph HP 6890 equipped with FID and autosampler, (b) column: 30 m × 0.32 mm ID fused silica capillary column, (c) stationary phase: HP-5 methylpolysiloxane with 5% phenylpolysiloxane, (d) film thickness: df = 0.23 μm, (e) supplier: Agilent. Because of the low concentrations in which the decomposition products of linoleic acid are present in the headspace, sampling was performed by SPME (solid phase microextraction). In this method, the volatile components from the gas phase were absorbed on the surface of a silicone-coated plastic needle and thereby enriched in the solid matrix. The molecules collected from the headspace were desorbed in the injector of the gas chromatograph subsequently employed.

Results and discussion

Complexation

Linoleic acid was found to build inclusion compounds with α-CD, β-CD and γ-CD, but only with α-CD was a complex easily formed by precipitation in 1:3 and 1:4 molar ratios (guest/CD) (Fig. 1). Due to the low water solubility of the complex, the excess α-CD, β-CD and γ-CD can be removed easily by a washing step. Using the kneading method, the complexation of a mixture of 0.4 mol of α-CD, 150 g water and 0.1 mol of LA was found to be complete at 70 °C within 2 h. The paste was dried at ambient temperature for 15 h and finally under vacuum at 50 °C for 2 h.

Stability tests

Various studies on linoleic acid were carried out to determine the appropriate cyclodextrin, optimum complex composition and the performance of the inclusion compound.

The results made clear that the cyclodextrin with the smallest cavity, α-cyclodextrin, provides the greatest stabilization effect. This is shown by comparing the storage stabilities of the different cyclodextrin/linoleic acid complexes (Fig. 2). The experiments were conducted using complexes with a water content between 2 and 10% by weight. The decrease in LA concentration was measured by proton NMR.

The 4:1 α-cyclodextrin/linoleic acid complex remains highly stable to light (Fig. 3) in decorative cosmetic

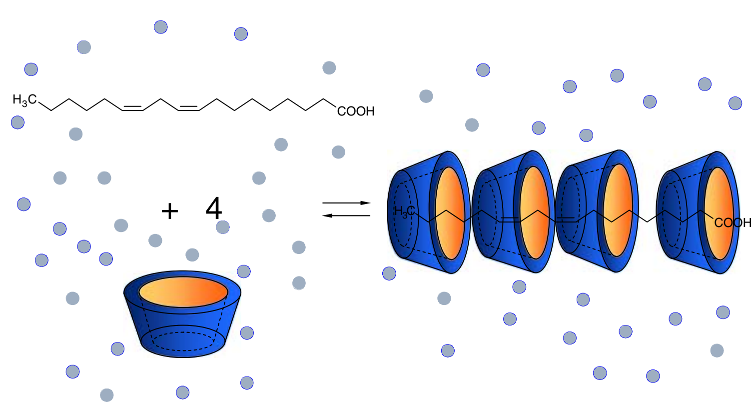

Fig. 1 Demonstrates how linoleic acid forms an inclusion complex with α-CD in a 1:4 molar ratio (guest/CD)

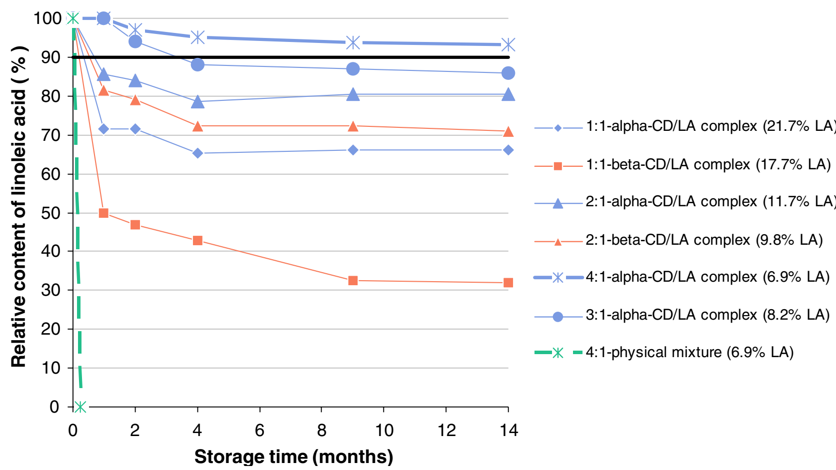

Fig. 2 Stability of cyclodextrin/linoleic acid complexes at 45 °C (stored in open containers)

formulations, such as face powder, eye shadow and foundation for more than 1 h. The uncomplexed linoleic acid deteriorates very fast in the color cosmetics. The decrease in LA concentration was measured by GC.

The sources of the rancid odor of formulations that contain linoleic acid were identified as pentanal, 2-hexenone, hexanal, valeric acid, 2-heptanone and caproic acid. SPME analysis detected these components in the gas space of cream formulations stored in closed jars under dark conditions at room temperature for 12 months. At the same time, the samples were evaluated by olfactory assessment. The odor intensity correlated particularly well with the hexanal content in the headspace. A cream with the 4:1 complex does not smell rancid even after 12 months' storage—unlike a reference formulation with free linoleic acid. The olfactory assessments reflect the hexanal concentration in the headspace above the creams.

The large area beneath the hexanal peak in the gas chromatogram is associated with an intense odor. Hexanal was therefore used as a marker for assessing the rancid odor. Because of the low concentrations in which the decomposition products are present in the headspace, sampling was performed by SPME.

The control formulation containing the unprotected form of linoleic acid was characterized by a very unpleasant off-odor after 12 months' storage (olfactory ranking: odor intensity 4), which correlated with nearly 10 times more hexanal content in the gas phase compared to the cream formulation containing 1% complexed linoleic acid.

Conclusion

Reversible complexation makes it possible for the first time to use linoleic acid in various cosmetic formulations and personal-care products. This means that vitamin F is made available for the first time by this method in a form that is stable to light, oxygen and

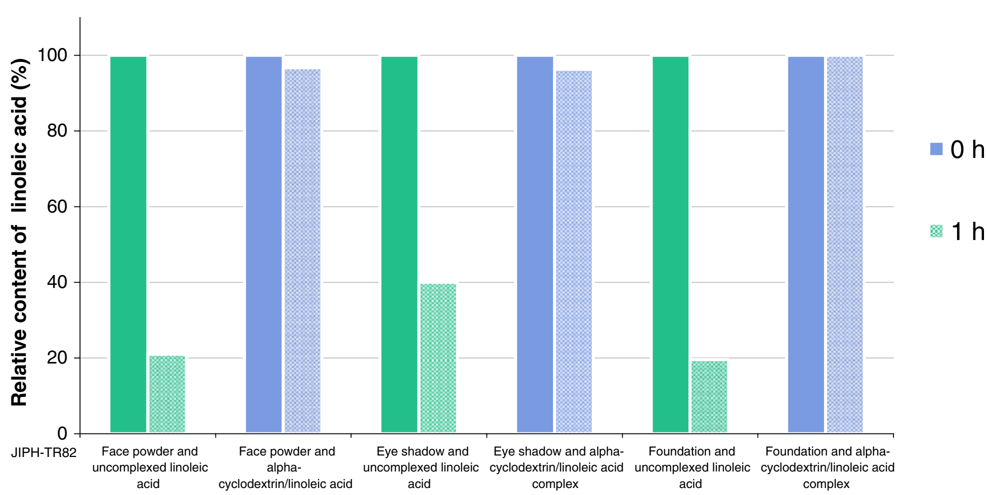

Fig. 3 UV stability of complexed (4:1) and uncomplexed linoleic acid in various decorative cosmetic products (1% linoleic acid, UV-A and UV-B sun test, 45 °C)

temperature, in a very efficient molecular inclusion complex for use in cosmetic products. Complexes of lipophilic vitamins can therefore be considered as ‘‘the world’s smallest beauty cases.’’

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